



# Newborn Screening Update for Health Care Practitioners

Changes in regulations affecting your practice for  
newborns transferred to neonatal intensive care  
units.

Department of Health & Human Services



## Changes for newborn screening of premature, sick and low birth weight babies admitted to NICU's.

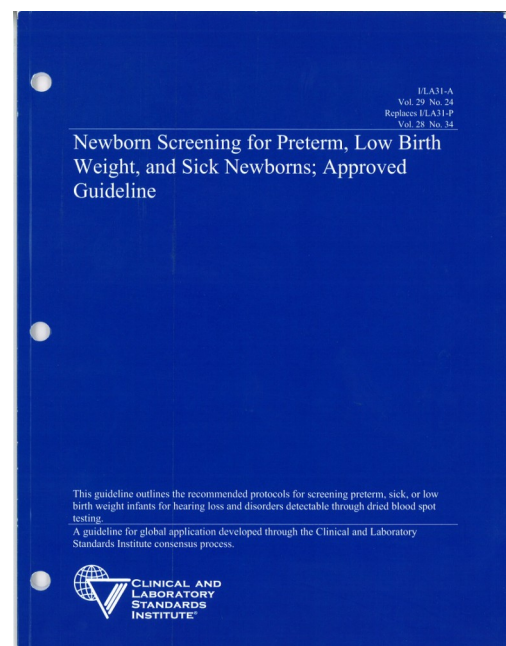
The Nebraska Newborn Screening Program “Regulations Governing Screening of Infants for Metabolic Diseases” are being revised to adopt practices consistent with the global guidelines of the Clinical and Laboratory Standards Institute on “Newborn Screening for Preterm, Low Birth Weight, and Sick Newborns” I/LA31-A. Hospitals will be notified of the effective date as soon as the regulations are signed by the Governor.

After careful consideration by the Newborn Screening Advisory Committee these changes are being made with the following considerations in mind:

Approximately 10% of all births involve babies who are either premature, low birth weight, have birth defects or are sick requiring they be transferred to neonatal intensive care units. There are approximately 26,000-27,000 births each year in Nebraska. Although the NICU population accounts for about 10% of births, they account for about 10-40% of the follow-up workload.

NICU babies are at greater risk for missed or incomplete NBS than normal newborns as this can be overlooked given the critical activities surrounding their care, and because treatments they receive, and the genetic and biochemical nature of the infants themselves can interfere with obtaining reliable results. Transfusions, parenteral nutrition, medications can all impact the validity of screening results and significantly delay or prevent diagnosis of affected newborns.

Because low birth weight babies have less blood volume and since testing for many things beyond newborn screening must often be done, it becomes even more important to optimize the timing and minimize the number of blood spot specimen collections.



## A day in the life of a premature NICU baby...



The neonatal intensive care unit has undergone several practice changes over the last few years which may influence interpretation of the newborn screen. Understanding a typical life for the preterm baby can help decipher the newborn screen results.

Immediately after delivery, the preterm infant (<37 weeks gestational age) is assessed for need to intubate or place on nasal cpap, oxygen, or room air (NRP). Many practitioners give exogenous surfactant either in the delivery room or in the NICU via an endotracheal tube to all infants < 28 weeks gestation every 6 hours as needed up to 4 doses.

The preterm infant is born with limited nutrient reserves yet has a heightened requirement for nitrogen balance and growth, therefore, provision of amino acids are given after delivery thereby, impacting the newborn screen. Intravenous lipids with a soybean emulsion begin within 24 hours to prevent essential fatty acid deficiency and augment caloric intake. The goal intravenous nutrition support is 80 non protein calories and 3-4 grams per kilogram body weight of protein. Fluid needs vary by birthweight. Sodium is avoided for the first few days until an active diuresis occurs. Calcium, phosphorus, trace elements are provided in standard amounts by day 1.

Because of the infant's immature cerebral vessels and risk for intraventricular hemorrhage, screening head ultrasounds are done initially by day of life 7. Blood pressure goals can be problematic and infants may be on exogenous hydrocortisone, dopamine or other pressors with known influence on newborn screen results. The fetal circulatory system runs in parallel with the patent ductus arteriosus (PDA) and may be problematic for the preterm infant trying to switch to a postnatal circulatory pattern that runs in series. Infants may be on prophylactic indomethacin or treatment courses of indomethacin or ibuprofen to try and medicinally close this PDA. Preterm infants often need blood transfusions with PRBC due to diminished erythropoiesis. Fresh frozen plasma and cryoprecipitate are often reserved for coagulopathy related septic events or bleeding disorders. Ampicillin and Gentamicin are often given in the first 2 days of life until infant blood cultures are negative for 48 hours.

Enteral nutrition begins typically via an orogastric tube by day of life 2-5 depending on the nursery involved. Human milk is the preferred milk because of its unique biology, bioactives, and nutritional properties and preterm infants have less sepsis, necrotizing enterocolitis on human milk. Feedings are initiated (<20ml/kg) and advanced by not more than 20 ml/kg/day to avoid feeding intolerance and or NEC. Human milk is fortified with commercially available products to augment protein, calcium and phosphorus and other micronutrients to provide for intrauterine accretion goals. If the preterm infant has no human milk source, then commercially designed preterm formulas are recommended which can be cow milk, intact protein sources with casein and whey amino acid profiles or recently a new whey hydrolysate formula has been designed for the preterm infant. The formulas contain a blend of MCT:LCT and a blend of glucose polymers : Lactose sugar. Infants do require 400 IU additional Vitamin D because of limited daily volumes and may also be on exogenous iron.

Finally, the preterm infant is often in the NICU for 3 months or near to the original due date. Throughout this time period, optimal strategies for evaluating for newborn screen disorders have been fraught with interpretation issues. Based on new knowledge of preterm care, newborn screening techniques, the new recommendations for newborn screening have been developed.

*Excerpt reprinted with permission from Clinical and Laboratory Standards Institute ILA31-A "Newborn Screening for Preterm, Low Birth Weight, and Sick Newborns; Approved Guideline"*

## Serial Screening of NICU admissions

The global guidelines specify and State regulations soon will require:

**1) Every newborn shall have a dried blood spot specimen collected prior to transfer to a NICU even when the baby is less than 24 hours of age.** (This is not new). The Nebraska Newborn Screening Program (NNSP)

Transfer form must be completed and sent with the baby, and faxed to the NNSP. The receiving NICU must **VERIFY** that the newborn screening specimen has been collected (this is new and should be written into hospital NICU procedures). If it cannot be verified, the NICU **MUST** collect a newborn dried blood spot specimen **PRIOR** to any treatments (e.g. transfusions or parenteral nutrition) – (excluding respiratory lifesaving treatment).

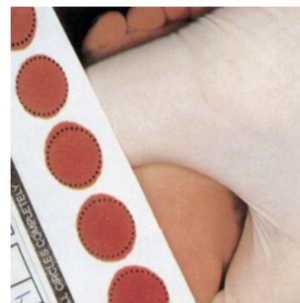
**2) If the initial specimen was collected @ < 24° a repeat specimen must be collected at between 48-72° of age.**

**3) If the baby was < 2000 grams at birth or < 34 weeks gestation, a third specimen shall be collected at 28 days of life or upon discharge whichever occurs first.**

### **First specimen:**

The advantages of collecting that first specimen before any treatments include obtaining reliable screening results for hemoglobinopathies, galactosemia and biotinidase deficiency. In addition baseline amino acid and acylcarnitine results can be obtained. Virtually all babies in the first 48 hours are catabolic, so fatty acid oxidation disorders are more likely to be detected.

The disadvantages include that early collected specimens are often associated with higher false positive results for TSH's for congenital primary hypothyroidism, 17-OHP's for congenital adrenal hyperplasia and IRT's for cystic fibrosis. However, with routine implementation of repeat specimens collected at 48-72 hours of age, normal results will usually be obtained on these. Unless the initial screen is substantially abnormal, the routine repeat should resolve concerns.



### **Second specimen:**

The advantages of collecting a routine repeat specimen at 48-72 hours of life on babies who's first specimen was collected at < 24 hours of life are: this specimen should give reliable results for congenital primary hypothyroidism, congenital adrenal hyperplasia, cystic fibrosis and most screened amino acid, organic acid and fatty acid conditions.

The disadvantage of the second specimen is that in babies receiving carnitine in parenteral nutrition (PN) formulas, carnitine disorders may be masked. Likewise fatty acid oxidation disorders can be masked if babies are receiving adequate nutrition and caloric intake due to the PN.

### **Third specimen:**

The advantage of collecting the third specimen on day 28 or on discharge whichever is first (for baby's who were < 2000 grams at birth or < 34 weeks gestation) are: Thyroid function is more likely to have matured to expected newborn levels, so screening at this time is more likely to be a reasonable measure of thyroid status. It might also improve chances of detecting babies with delayed TSH rise, later onset CAH and homocystinuria in preterm infants. In addition, usually by this time PN has been discontinued, and abnormal patterns frequently found in earlier specimens (e.g. multiple amino acids elevated), will have normalized.

### **Are these babies really at risk?....**

In Nebraska each year, about 50 babies (54 in 2009) are identified through screening, diagnosed, and treated in time to prevent intellectual disability, other health problems and avoid premature death. Babies in NICU's are at no less risk than babies from the normal newborn nursery. Some examples from the past few years (2004-2010) include:

- A 1475 gram, 35 week gestation baby diagnosed with methylmalonic acidemia.
- A 1820 gram, 37 week gestation baby diagnosed and treated by day 8 with congenital primary hypothyroidism.
- A 1045 gram, 27 week gestation baby diagnosed with cystic fibrosis. The initial screen prompted a repeat specimen which had already been collected by the time

- A 530 gram 23 week gestation baby with congenital primary hypothyroidism. The first specimen was drawn early prompting a repeat. The repeat was collected on day 11 diagnosis and treatment started day 16
- A 545 gram 23 week gestation baby diagnosed with congenital primary hypothyroidism. The repeat specimen was collected at > 24 hours without delay which identified a low T4/ high TSH prompting confirmatory testing and diagnosis. Treatment was initiated by day of age 8.
- A 3090 gram, 34 week gestation baby with the first specimen collected at <24° had a C8 (octanoylcarnitine) substantially above normal & 2 copies of the mutation commonly associated with classical Medium Chain Acyl Co-A Dehydrogenase Deficiency (MCAD). Reported out day of life 3. Repeat on day 3 substantiated and diagnosed MCAD. (Discovered, previous sibling had expired with SIDS). Intervention initiated on day of life 3.
- A 1522 gram 30 week gestation baby. NICU was notified on day of life 7 of a positive 17-OHP screen. Confirmatory steroid profile collected day of life 8, and results confirmed CAH by 22 days. In the meantime, NICU knew to monitor electrolytes.

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